

Atty Dkt. No.: 10010632-3  
USSN: 10/611,409

### **REMARKS**

In view of the following remarks, the Examiner is requested to allow Claims 21-34, 42 and 43, the only claims pending and under examination in this application.

Claims 21, 22, 42 and 43 have been amended to clarify the claim language. Support for these amendments can be found throughout the specification and claims as originally filed, e.g., as developed in greater detail below. Accordingly, no new matter has been added.

As no new matter has been added by way of these amendments, entry thereof by the Examiner is respectfully requested.

### ***Claim Rejections – 35 U.S.C § 102***

Claims 21-31, 33-34 and 42-43 have been rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Schmidt et al. (WO 99/02728).

According to the M.P.E.P. a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. The identical invention must be shown in as complete detail as is contained in the claim. See M.P.E.P. § 2131.

Claim 21 is directed to a method of determining a nucleic acid sequence. The method includes the steps of:

- a) hybridizing a primer nucleic acid to a template nucleic acid,
- b) extending the primer by at least one complementary nucleotide that includes a 3' cleavable tag to produce an extension product,
- c) cleaving the 3' cleavable tag from the extension product to produce:
  - 1) a cleaved tag, which is not bound to the nucleotide, and
  - 2) an extension product that includes the at least one complementary nucleotide which is hybridized to the template nucleic acid sequence; and

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d) detecting the cleaved tag away from the extension product to determine the nucleic acid sequence.

Accordingly, an element of Claim 21 is the production of an extension product that includes the at least one complementary nucleotide that is hybridized to the template nucleic acid sequence.

Schmidt does not teach a method of determining a nucleic acid sequence that results in the production of a cleaved tag and an extension product, wherein the extension product includes the at least one complementary nucleotide that is hybridized to the template nucleic acid sequence.

Schmidt does not teach this because in the Schmidt method a population of tagged extension products is produced, the population of tagged extension products is dissociated from template nucleic acids, then the individual extension products are separated on the basis of their length, and it is only after the individual extension products have been separated based on their length that the tag is cleaved and detected. See page 2, last paragraph continuing on to page 3. Hence, in the method disclosed by Schmidt, prior to cleavage and detection of the tag the extension product is dissociated and separated from the nucleic acid template. Specifically, Schmidt discloses that the extension products are dissociated from the nucleic acid template and separated one from another via capillary electrophoresis. See page 45, first full paragraph:

are shown in Figure 15. Prior to cleavage of labels one needs to separate the Sanger ladder into its component fragment lengths. In a mass spectrometry system this stage can be coupled to the sample loading in a LCMS system. Separation into bands can be achieved by capillary zone electrophoresis. This will then pass through a UV spectrometer to determine the quantity of DNA in each band. Following this the sample will then pass through a photocleavage module to release the mass-labels which will then be injected into an electrospray mass spectrometer for analysis of the labels in each band.

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Accordingly, because Schmidt discloses that the extension product is to be dissociated and separated from the nucleic acid template prior to cleaving the cleavable tag from the nucleic acid, the method of Schmidt does not include the production of a cleaved tag and an extension product which includes the at least one complementary nucleotide that is hybridized to the template nucleic acid sequence. In other words, in accordance with the Applicants methods, the extension product is not removed from the hybridization reaction mixture prior to cleavage of the tag.

The Office argues that Schmidt discloses this element because Schmidt discloses the limitation of "cleaving a 3' cleavable tag from the extension product to produce a cleaved tag and an extension product that includes at least one complementary nucleotide that is hybridized to the nucleic acid sequence' because Schmidt et al. disclose that the nucleic acid fragments which are extended product [sic] and are separated."

However, as explained in detail above, Schmidt actually teaches that the extension products are dissociated from the template nucleic acid and separated based on their length via electrophoresis prior to the cleavage of the tag from the extension product. Accordingly, because the extension product is dissociated and separated from the hybridization mixture that includes the template nucleic acid, Schmidt does not teach the production of a cleaved tag and an extension product which includes the at least one complementary nucleotide that is hybridized to the template nucleic acid sequence. Rather, Schmidt discloses the production of a cleaved tag and an extension product that has been dissociated from the template nucleic acid and subjected to electrophoresis.

Therefore, Schmidt does not anticipate the claims, because it fails to teach every element of the rejected claims. Hence, the Applicants respectfully request that the 35 U.S.C. § 102(b) rejection of Claims 21-31, 33-34 and 42-43 be withdrawn.

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***Claim Rejections – 35 U.S.C. § 103***

Claim 32 has been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Schmidt (WO 99/02728) in view of Cheeseman (U.S.P.N. 5,302,509).

According to the M.P.E.P. § 706.02 (j), to establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

The Office acknowledges that Schmidt is deficient in that it fails to teach a fluorescent cleavable tag. Accordingly, the Office relies upon Cheeseman to remedy the deficiencies of Schmidt. However, as set forth above, Schmidt is deficient in that it fails to teach or suggest the production of a cleaved tag and an extension product which includes the at least one complementary nucleotide that is hybridized to the template nucleic acid sequence. As Cheeseman was cited solely for its disclosure of a fluorescent cleavable tag it fails to remedy the deficiencies of Schmidt. Hence, a *prima facie* case of obviousness has not been established because the recited combination fails to teach every element of rejected Claim 32. Accordingly, the Applicants respectfully request that the 35 U.S.C. § 103(a) rejection of Claim 32 be withdrawn.

***Claim Rejections – 35 U.S.C. § 112, first paragraph***

Claim 43 has been rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing new matter.

In making this rejection, the Office asserts that there is no support in the Applicants' specification for the phrase "to produce a hybridization product composition." Without in any way agreeing with the position of the Office, the

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Applicants have amended the claim to refer to "sample," which is a term fully supported in the specification. See e.g., the discussion at page 18, line 7.

In view of the above amendment to Claim 43, this rejection may be withdrawn.

***Claim Rejections – 35 U.S.C § 112, second paragraph***

Claims 43 and 22-24 have been rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

According to the M.P.E.P. § 2173.03 the test for determining whether a claim complies with 35 U.S.C. § 112, second paragraph, is whether the claim apprises one of ordinary skill in the art of its scope and, therefore by providing clear warning to others as to what constitutes infringement of the patent.

Claim 43 has been rejected because the Office alleges that the phrase "a hybridization product composition" is unclear. In view of the removal of this language from the claim, this rejection may be withdrawn.

Claims 22 to 24 have been rejected as allegedly vague and indefinite because the phrase "a single cleavable tag terminated deoxynucleotide triphosphate" is allegedly unclear. Without in any way agreeing with the position of the Office, Claim 22 has been amended above to track the language of the specification at page 5, lines 2 to 3. Therefore, the Applicants respectfully request that this rejection be withdrawn.

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**CONCLUSION**

Applicant submits that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone Bret Field at 650-833-7770.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-1078, order number 10010632-3.

Respectfully submitted,

Date: February 13, 2007

By: 

James S. Nolan  
Registration No. 53,393

Date: February 13, 2007

By: 

Bret E. Field  
Registration No. 37,620

AGILENT TECHNOLOGIES, INC.  
Legal Department, DL429  
Intellectual Property Administration  
P.O. Box 7599  
Loveland, CO 80537-0599

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